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CENTENARY OF PAVLOV'S BIRTH

BY

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Ivan Petrovich Pavlov was born a hundred years ago in Ryazan, a district town in Central Russia. He died in 1936, one of the great men of his time, of immense prestige in his own country and famous throughout the world for his scientific achievements. We are too close to him to forecast the verdict of future generations, or rather to know which phase of his work will seem the most important, but we are fortunately not too far off to remember what he was like. Many of us have witnessed the energy, the sincerity, and the buoyant enthusiasm which made him such a universal favourite. He was a great character—outspoken, impatient, and fiery-tempered, with an engaging simplicity and delight in work and play.

To the physiologist, Pavlov's work covers several fields and goes back almost to the beginning of the modern era, to the time of Ludwig and Heidenhain. To the world at large it has come to be identified with the single bold conception of the conditioned reflex. The idea that intelligent behaviour might be reduced to such a basis was welcomed by some as a new and inspiring philosophy and dismissed by others as wicked nonsense. It was seldom viewed as the working hypothesis for a new kind of experiment. It was like Pavlov to take such a novel and simple generalization as the basis for his work on the brain, but in the end the generalization may have less importance than the facts it produced. And even if Pavlov had never worked on the brain he would still have been one of the outstanding physiologists of his age. He had won the Nobel prize for his researches on digestion at a time when his conditioned reflex experiments had scarcely begun.

An excellent account of Pavlov's career has been given by his old pupil, Professor Anrep (1936). He was the eldest son of a parish priest and was a vigorous child, delighting in all forms of physical achievement. An accident postponed his schooling and he was not particularly distinguished as a scholar, but in 1870 he entered the Faculty of Science of the University of St. Petersburg and came under the influence of Cyon, who was then professor of physiology. Cyon, the discoverer of the cardiac depressor nerve, suggested a problem on the innervation of the pancreas, and Pavlov did so well in his first research that he was awarded the gold medal of the University.

Experimental Work

In 1875 Cyon was elected as professor at the Medical Academy and took Pavlov as his assistant, but the election was revoked by the Government. Pavlov indignantly refused to serve under Cyon's successor and moved to the Veterinary Institute. In 1879 he became medically

qualified, and a few years later he completed his training by working in Germany with the two leaders of experimental physiology—Ludwig, the exponent of precise method in the study of the circulation, and Heidenhain, the investigator of secretory processes. Under their influence, on his return to Russia he settled down to work first on the innervation of the heart and then on the secretion of the digestive glands.

He was already an experimental surgeon of great dexterity, and he had come to realize that in the study of normal digestion the well-being of the animal was essential. Discomfort and anaesthesia were both eliminated, and his dogs were trained to co-operate fully in the experiment. The result was a revolution in the technique of investigating the digestive tract. There were the sham feeding method, the innervated Pavlov pouch, and the Eck fistula, and all his work revealed a direct grasp of essentials and a mastery of experimental detail. He discovered the secretory nerves of the stomach and pancreas, the acid control of the pyloric sphincter, the nervous and chemical phases of gastric secretion, and the action of enterokinase. In fact, most of our present knowledge of the physiology of digestion is based on the work done in Pavlov's laboratory between 1888 and 1906. In 1904 he was awarded the Nobel prize for this work, and in 1907 was elected a Foreign Member of the Royal Society.

It is sometimes said that the discovery of secretin by Bayliss and Starling in 1902 made Pavlov realize that future work on the digestive system would lie with the physiological chemist. But his decision to turn from the study of digestion to that of brain function was probably inevitable. The nervous control of digestion always interested him far more than the chemical, and he had already discovered a kind of nervous control which cried out for further investigation. The secretion of saliva was produced reflexly by food in the mouth or by the smell of food, but it was also produced by the sight of food—i.e., by a visual pattern customarily associated with feeding. Pavlov called this the psychic secretion. He soon found that the stimulus need not be visual; the sound of the dinner bell could be made just as evocative as the sight of the dinner. In fact, the dog could be trained so that it would salivate to a particular stimulus or combination of stimuli which had no necessary connexion with food. The reaction had the almost mechanical certainty of the reflex, but it depended on the higher levels of the nervous system. Although expressed by the secretion of a digestive gland, it seemed to be on a par with other kinds of behaviour involving learning, recognition, and intelligence.

Conditioned Reflexes

From 1905 onwards Pavlov settled down to investigate these conditioned reflexes, and for the rest of his life he was constantly at work on them. We do not yet know what neural processes take place in the brain when a new habit is formed, but what we do know about animal and human behaviour has been enormously extended by what Pavlov found out. He used a new method of experiment and a new way of treating the results. Thorndyke had studied the associative processes in animals by experiments in which the solution of a simple problem was rewarded by food. His results were published in 1898 in his book, *The Animal Intelligence*, which is now one of the classics of experimental psychology. Pavlov studied the formation of reactions associated with feeding, but he deliberately excluded the subject-matter of psychology. He believed that the physiologist ought to keep to his proper sphere, that nothing but confusion would come if he began to speak or think of learning, of fears and hopes, success or failure. He must confine himself to an objective analysis of the external stimuli and of the animal's behaviour. He must "adhere strictly to the physiological point of view, investigating and systematizing the whole subject by physiological methods alone." This is easier said than done: the exclusion of the familiar terms which we use to describe our own behaviour often seems to involve a complex restatement in which half the picture is left out. But Pavlov adhered strictly to his principle, and was justified by the discoveries which it brought. He set himself to study not "learning" but the "formation of conditioned reflexes," and he succeeded in demonstrating many of the rules which govern their formation.

Pavlov has been praised or blamed because his thesis could be taken to mean that men are machines and should be treated as such. Naturally he wanted to see how widely his physiological net could be cast, and he was human enough, one might almost say naughty enough, to enjoy the reaction of his hearers when he discussed religion as an example of the social conditioned reflexes. But his real concern was with the experiments he was making to cover the borderline between innate and acquired reactions. The value of his way of approach is shown not only by what he himself found out but by the whole development of behaviour studies in the past thirty years.

There is no doubt at all about the value of the method. The conditioned reflex is now used as one of the standard tools for investigating the capacity of the nervous system. It can be used to study the range of sensory discrimination, the effects of cerebral injury, etc., for Pavlov has shown how conditioned reflexes can be formed and kept in being, and for many purposes that is enough. We need not try to understand the underlying changes which must have taken place in the nervous system.

A Good Working Hypothesis

There is naturally more doubt about the detailed scheme which Pavlov elaborated to account for his findings. It invoked a number of special processes assumed to take place in the brain—irradiation, positive and negative induction, extinction, inhibition, and generalization. It became more elaborate as the work progressed. The cortex was thought of as a mosaic of excitatory and inhibitory points with further excitatory and inhibitory influences spreading out by irradiation or concentrated in particular regions. The scheme is difficult to follow, partly because some of the terms carry unfamiliar meanings and partly because Pavlov was constantly adding to it. It had to reconcile

a vast number of experimental results, and we may be sure that it was never wholly satisfactory to its originator. But for Pavlov it certainly fulfilled the function of a good working hypothesis in that it was continually leading to fresh investigations; it was a spur to his original genius, but was not without danger to the many pupils who were dominated by his thought. Like so many biological theories it became a dogma not to be challenged except in inessentials, and so prevented the fusion of the brain physiology of Pavlov's school with that studied in other countries by different methods and from a different starting-point.

There were, of course, many other reasons to prevent a complete interchange of ideas, and it is a mistake to suppose that Pavlov's views have been immune from criticism in his own country. His genius would have dominated less ardent minds wherever he had happened to work; in the U.S.S.R. Beritoff has been an outspoken critic for many years, and Anokhin and Kupalov have both upheld objections on specific points. Fortunately a monograph has now been published by Konorski (1948), an old pupil of Pavlov's, which will help to remove the misconceptions which have grown up. It is a criticism of Pavlov's scheme and an attempt to bring his work into line with recent neurophysiological research, but it also gives an impressive picture of the range and exactitude of the experiments of his school and of the hard thinking which went to their interpretation. Konorski finds Pavlov's scheme inadequate because the original conceptions were never clearly defined and so could be used, and often were used, to mean different things. He says, "For as long as the great edifice of knowledge built up by Pavlov was guided and extended under that great scientific genius it could continue to grow despite its isolation and despite the fundamental inadequacy of its construction"; but he feels that "Pavlov's priceless heritage" will be lost if there is no synthesis with other lines of advance in the physiology of the nervous system.

"Use Facts and Do Not Theorize"

It is doubtful whether a complete synthesis can be made without first pulling down much of the edifice which has been built up so carefully, but this does not mean that the work was wasted. Anrep tells us that theoretical interpretations in general had little value for Pavlov: "Use facts and do not theorize," was his constant saying. He has given us a host of facts relating to the plasticity of the brain, and the facts were selected to reveal the general principles of habit formation, not to vindicate a particular theory of cortical activity.

Pavlov worked on conditioned reflexes for the last 30 years of his life. He had neither the time nor the temperament required for the lengthy experimental work; indeed, Anrep records that Pavlov never attempted to establish a conditioned reflex himself, but he was in close touch with the many experiments going on under his direction. The work was constantly expanding into newer and larger institutes, yet he was able to manage them and to direct a host of research workers without losing contact with their problems. He could do this because he had immense reserves of physical energy and was able to switch his mind completely and without effort to the task before him. He could be the scientist, the administrator, the family man, the gardener, the book collector, or the naturalist. He could fill each role with enthusiasm. He could be a charming host or guest in spite of language barriers.

Many physiologists will remember the impressive sincerity of his presidential address to the International Physiological

Congress in Leningrad in 1935. He warned us that the ties of international science would not be strong enough to prevent war, though war is "essentially a bestial method of settling difficulties, a method unworthy of the human mind with its unlimited resources." But the Congress promised new friendships and was altogether a splendid affair, a fitting tribute to its world-renowned president. He was in his 86th year, a venerable but not an aged figure. He died six months later, after a short illness.

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MYXOEDEMATOUS MADNESS

BY

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Myxoedema is one of the most important, one of the least known, and one of the most frequently missed causes of organic psychoses—important because it may respond so gratifyingly to treatment, little known because little has been written about it, often missed because the textbook description of myxoedema is not the rule but the exception.

Fourteen cases are here described, all of which had myxoedema and psychotic changes. In every one of them the diagnosis was confirmed beyond doubt. They all showed a psychosis amounting to complete "madness," ten being admitted to the mental observation wards under the Lunacy Act, one referred to the neurosurgeon for cerebral tumour, and three to general medical wards with other diagnoses. In nine of the cases there was a dramatic and complete recovery of sanity with thyroid treatment, in two there was partial improvement, one showed no change, and two patients died. The fact that in none of these cases had the diagnosis been made by the outside doctor suggests that there is need for increased awareness of myxoedema as a cause of psychoses, and, further, shows that it may be worth while discussing how myxoedema can be diagnosed so that cases may be recognized and treated early.

The average doctor is well aware that dullness and a poor memory are caused by myxoedema, but does not realize that a frank psychosis can occur. Dr. Leonard Simpson, in Price's *Medicine*, describes the condition clearly and stresses its importance, but most of the popular textbooks omit any reference to it at all, and this may account for the rarity of its recognition. Apart from medical textbooks, A. J. Cronin (1937) paints a vivid if sensational picture of a "mad myxoedema," and it was from this source that I first learned of the condition. Though Stoll (1932) described six personal cases, the fact that Zondek and Wolfsohn (1944) published one solitary case of myxoedematous psychosis in 1944 suggests again that it is regarded as a rarity. Nevertheless, the condition was clearly described, and was recognized as exceedingly common by the Committee of the Clinical Society of London (1888) appointed in 1883 to consider the subject of myxoedema. Their report says (p. 31): "Delusions and hallucinations occur in nearly half the cases, mainly where the disease is advanced. Insanity as a complication is noted in about the same proportion as delusions and hallucinations. It takes the form of acute or chronic manias, dementia, or melancholia, with a marked predominance of suspicion and self-accusation." (At the time

of that report thyroid treatment was quite unknown, so doubtless many of the cases would to-day have been diagnosed and treated before mental symptoms arose.) I want to make it clear that I am not describing something new, but something old that is nowadays often forgotten.

Is there a Specific Type of Psychosis Associated with Myxoedema?

This question is fully discussed by Akelaitis (1936). The possible theories are: (1) that myxoedema produces a psychosis depending on the "pre-psychotic reaction type"; (2) that it produces a specific type of psychosis; and (3) that it produces psychoses of various types, either resembling one of the ordinary idiopathic psychoses or else typical of no special type.

Cases in the literature record a very wide variety of mental changes, and certainly in the series I have observed there has been no constant type of psychosis, though general confusion and disorientation with persecutory delusions and hallucinations, and occasional bouts of restless violence, have been common. I have made the diagnosis on the myxoedematous appearance of the patient and not on the kind of mental symptoms. No physician would attempt to diagnose lobar pneumonia or typhoid by the delirium they may produce, and likewise in myxoedema it is the disease which is the characteristic feature, not its mental manifestations.

The fact that recorded cases of myxoedema psychosis have closely resembled paranoia (Case 1 and Stoll, 1932), schizophrenia (Zondek and Wolfsohn, 1944), melancholia (Buschan, 1896), or other orthodox psychoses does suggest that the common psychoses—schizophrenia, mania, melancholia, paranoia, and so on—may turn out to be not diagnoses in themselves, but manifestations of underlying organic disease.

Does the Response to Thyroid Prove the Myxoedematous Origin of the Psychosis?

First, if the case responds it is of course no absolute proof, because almost any type of psychosis can improve spontaneously. Nevertheless, when mental symptoms that have been present in a hypothyroid patient for many months clear dramatically within a few weeks of starting thyroid it is reasonably certain that they were due to myxoedema.

Secondly, if the mental changes persist after adequate thyroid treatment, does this mean they were not myxoedematous? As Ruhberg (1936) points out: "It is necessary to determine if they are secondary to thyroid insufficiency or merely a coincident concomitant." He states dogmatically: "If the mental symptoms are part of myxoedema, improvement and relief should be obtained by establishing a normal basal metabolic rate." Akelaitis (1936), discussing cases which showed physical but not mental improvement with thyroid, also concludes: "The psychosis was a coincidence and not part of the myxoedema." Such dogmatic assumptions are unjustified. It is generally agreed that metabolic changes can produce irreversible damage—for instance, the changes of prolonged hypoglycaemia or of pellagra may fail to respond respectively to glucose or to the vitamin B complex, although they were caused by deprivations of these. Again, the belated treatment of cretinism shows that the changes in the brain cannot be reversed by thyroid.

Dr. Leonard Simpson (personal communication) records such a case in which peculiar behaviour persisted after thyroid treatment and ultimately ended in psychosis. Hence